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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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0.129,951 01/16/98 MILLS

A LITEC0008

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HW12/1219

EXAMINER

MARSCHER, A

ART UNIT	PAPER NUMBER
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1631

17

DATE MAILED:

12/19/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/129,958

Applicant(s)

Mills, Jr., et al.

Examiner
Ardin Marschel

Group Art Unit
1631



☒ Responsive to communication(s) filed on Sep 25, 2000

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1035 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 9-13, 15, and 17-28 is/are pending in the application.

~~Of the above, claim(s) 1-8, 14, and 16 have been canceled. is/are withdrawn from consideration~~

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 9-13, 15, and 17-28 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

Applicants' arguments, filed 9/25/00, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

If applicant desires priority under 35 U.S.C. § 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. It is noted that this appears as the first sentence of the specification following the title. The status of non-provisional application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Claims 11-13, 15, 17-24, 27, and 28 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amendment to claim 11, line 9, contains NEW MATTER.

Applicants pointed to the specification at page 33, line 23, through page 34, line 4, for written support for this amendment and incompletely summarized the content of that citation. The enzyme which therein is cited as removing a phosphate is the specific enzyme, bacterial alkaline phosphatase, and not merely a phosphatase as generically described in applicants REMARKS. Also, the enzyme which is therein cited as adding a phosphate group is not simply a polynucleotide kinase but rather at page 34, lines 3-4, is written as bacteriophage T4 polynucleotide kinase. Thus, said amendment to claim 11 at line 9 is broader than the written support as filed and therefore contains NEW MATTER via the increased breadth over the disclosure as filed. It is acknowledged that it may be obvious that the removal of a phosphate may be performed by a variety of phosphatases, for example, but what is obvious does not meet the written description requirement for amendments under 35 U.S.C. § 112, first paragraph. See, for example, the legal decision regarding NEW MATTER of In re Winkhaus, Tusche, and Kampf [188 USPQ 129(CCPA 1975)] at page 130, second column, section entitled "The § 132 Rejection" and section [2] on page 131. This rejection also applies to claims that depend from claim 11 via their dependence.

Upon reconsideration, the amendment to claim 9, last 3 lines, also contains NEW MATTER. In these lines the matrix

algebra result is stated as giving an analog result which is quantitatively dependent on the concentrations of at least one set of single-stranded oligomers. These limitations contain NEW MATTER regarding the following limitation: analog result of a matrix algebra operation which is quantitatively dependent on oligomer concentrations. Consideration of the instant disclosure as filed reveals that matrix algebra is described specifically only on pages 36-40 in two sections therein. The section starting on page 36 entitled "Product of a Matrix and a Vector" is the first section which describes concentrations on page 36, lines 10-14, but only regarding the input vector. No further concentration citation is present in this section which therefore lacks written basis for a analog result of a matrix operation being dependent, quantitatively or not, upon the concentrations of oligomers. The second section starting on page 39 entitled "Product of two Matrices" lacks any method disclosure per se and lastly indicates that this operation is not useful thus also failing to support the amendment. It is noted that applicants have not pointed to support for this amendment to claim 9. This rejection also applies to claims dependent from claim 9 via their dependence.

The amendment to claim 17, part (c), contains NEW MATTER regarding the phrase "the number of X_i oligomers for at least one basis vector e_i is greater than..." in that the limitation

therein directed to "at least one basis vector e_i is greater" has not been found as filed nor in the citations pointed to by applicants on pages 49 and 50. It is acknowledged that the sub-stoichiometric limitation regarding E oligomers versus X oligomers has written basis as filed but not the focus on the "at least one basis vector e_i ". This "at least one basis vector" limitation is therefore NEW MATTER. This rejection also applies to claims which are directly or indirectly dependent from claim 17 via their dependence.

Claim 27, lines 11-13, and claim 28, lines 13-15, contain NEW MATTER in that the limitation that the different basis vectors do not hybridize has not been found as filed. Consideration of the support, cited by applicants, on pages 27 and 28 reveals that the "do not hybridize" limitation is not anywhere disclosed therein. In fact, on page 27, lines 10-14, exactly the opposite is disclosed wherein the basis components for different vectors "do" hybridize and this is utilized for removal from a set of single-stranded oligomers. On page 28, lines 7-12, basis vectors are described as having minimal overlap and being not fully complementary but these descriptions do not correspond to or support the rather strong phrase "do not hybridize". Thus, the above noted limitation is clearly NEW MATTER in claims 27 and 28.

Claim 13 is rejected under 35 U.S.C. § 112, first paragraph,

because the specification, while being enabling for vector addition wherein the vectors are exactly oppositely oriented, does not reasonably provide enablement for any vector addition, such as for vectors that are not oppositely oriented in their vector space. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims. It is noted that the last 4 lines of claim 13 result in hybridization and removal of those oligomers which contain are complementary. These hybridized oligomers are removed leaving as the sum any leftover oligomers. Thus, the smaller vector in such addition removes its represented length from the oligomer mixture leaving any leftover amount from the larger vector. This resultant sum is only the vector addition result when the vectors are exactly oppositely oriented. Thus, this opposite orientation of vectors is the only enabled embodiment of this claim and not the generic vector addition as given in lines 1-2 of claim 13. This rejection is maintained and reiterated from the previous office action, mailed 5/23/00, because the claims lack a limitation that is important and is only stated in arguments but not in the claims. That limitation is that the various basis vectors of each vector to be added must be represented by oligomers which only hybridize under the conditions of the performance of the claimed method if the

oligomers represent the corresponding or same basis vector components between the vectors to be added. This is expressed in applicants' REMARKS on page 16, lines 3-4, filed 9/25/00, regarding therein exemplified basis vector hybridization but is not anywhere in claim 13 nor claims from which claim 13 depends. Thus, claim 13 is still so generic regarding vector addition that it lacks description of this basis vector hybridization restriction. Thus, claim 13 is still rejected under this scope rejection.

Claims 27 and 28 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for inner product determination wherein the vectors are exactly co-oriented, does not reasonably provide enablement for any vector inner product determination, such as non-co-oriented vectors. It is noted that the rate of hybridization is measured in order to obtain the inner product but there is no corresponding restraint placed on the single-stranded oligomers of the respective vectors which causes their hybridization to be controlled corresponding to vector orientation. That is, orthogonal vectors should not hybridize at all via made up of non-complementary oligomers so that the required zero output is obtained. No such oligomer limitations are given in the claim. Also, some amount of colinearity would give a non-zero inner product result but this would require some hybridizability at least proportional to the

orientation of the respective vectors relative to each other. No such limitations are present in these claims thus supporting this lack of scope of enablement rejection. This rejection is maintained and reiterated from the previous office action, mailed 5/23/00. Applicants firstly summarize the basic vector inner product mathematics and oligomer practice as described in the instant specification and corresponding to a textbook section as cited. This is acknowledged. Applicants then argue that the claims have been amended to require the non-hybridization of the basis vectors. Unfortunately, this has been noted above as being NEW MATTER and thus this rejection is maintained in anticipation of removal of the NEW MATTER thus leaving the claims rejected as before.

Claim 15 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 15, lines 1-2, directs the claim practice to "obtaining the outer product matrix of two vectors" and then only cites the obtaining of a set of oligomers without any step that enables either preparation of dimeric oligomers as given in the penultimate line of claim 15 nor enables what generates the outer product. This rejection is maintained and reiterated from the previous office action, mailed

5/23/00. Applicants argue that two methods of outer product practice are taught in the specification. It is acknowledged that the first method is taught regarding 5'-phosphate removal followed by ligation etc. The alleged second method as argued on page 21, lines 1-4, of the REMARKS, filed 9/25/00, citing also page 14, lines 22-25, only seems to describe method of oligomer synthesis, such as would be required for synthesizing the basis vector oligomers and does not describe a outer product practice. Thus, it seems that only "one" method of outer product practice is described and enabled thus supporting this rejection as not claiming any significant steps by which to achieve the outer product result since even the steps for this one method are not present in claim 15.

Claims 17-26 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 now has been amended to define the "sub-stoichiometric" limitation relative to X_1 oligomers and also relates "complete" to X_1 oligomers also regarding the E oligomers. These limitations confusingly conflict in that they seem to indicate that the E oligomers are both a "complete" set relative to X_1 oligomers as well as "sub-stoichiometric" which indicates less than a complete set. This rejection also applied

to claims dependent either directly or indirectly from claim 17 due to their dependence.

Claims 25 and 26 are vague and indefinite in that claim 25, lines 15-18, contain the conflict that the oligomers are described as being both "dimeric" and "single-stranded". The term "dimer" in the nucleic acid art is utilized to indicate a hybrid between two single-strands of nucleic acid formed via their complementarity. Thus, a dimeric oligomer and a single-stranded oligomer conflicts as to its form. It is suggested that, if applicants wish the claim to cite only single-stranded oligomer forms in the claimed memory composition then replacing "dimeric" with a phrase such as "capable of hybridizing to form a dimer" would clarify the claim that dimers are not present in any embodiment of the claimed memory. On the other hand, if dimers are meant to be present in the claimed memory composition then the "single-stranded" wording needs to be changed to a capability type limitation. Clarification as to the metes and bounds of the form of the oligomers in the claimed memory is requested via clearer claim wording.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or

on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9-11 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by either Adleman(Science 266:1021[1994]), Guarnieri et al.(Science 273:220 [1996]), or Oliver (J. Mol. Evol. 45:161[1997]).

This rejection is maintained and reiterated from the previous office action, mailed 5/23/00. Applicants firstly argue that Adleman does not employ oligomers representing both positive and negative values as well as the abstracts of Guarnieri et al. or Oliver. In response applicants' invention is directed to methods wherein components of the vectors therein are utilized to represent data as supplied in determining a mathematical result. It is acknowledged by applicants at various points in arguments as also from the instant specification that the vectors may not always have both positive as well as negative components, especially the negative ones. That is, if the input data only contains positive vector components as are utilized in the references then the set of oligomers which are practiced in the method are all positive and still fall within the instant invention practice. Again the instant claims do not limit the component values of the input data and thus are deemed to include positive only vector component practice as is also present in the references. Applicants argue further regarding the analog result of matrix algebra being quantitatively represented by the

concentrations of the E oligomer sets as not being disclosed in the references and now a limitation of the rejected claims. This limitation has been noted above as being NEW MATTER. Thus, this rejection is maintained in anticipation of removal of the NEW MATTER thus leaving the claims rejected as set forth in the previous office action, mailed 5/23/00.

Claims 25 and 26 are rejected under 35 U.S.C. § 102(b) as being anticipated by Southern (WO 89/10977).

It is noted that claims 25 and 26 are composition claims directed to content-addressable memory claimed with product by process limitations. Applicants are reminded that such products which may be made by other, possibly completely, different processes may be subject to rejections over prior art which discloses the claimed product(s). In this case consideration of claims 25 and 26 reveals that they are directed to products which are the result of vector mathematical manipulations set forth in the claims as resultant from the formation of an outer product between certain vectors. It is also noted that the claims are not limited in any way as to what vectors are initially utilized for the formation of said outer products. Thus, the components which are in the memory span a vast expanse of possible outer product results. The only limitation is that at least some minimal pool of single-stranded oligomers comprising a set of dimeric oligomers must be present and that it must be content-

addressable. Dimeric, albeit unclear as noted above, will be assumed for the purposes of this rejection to indicate that each dimeric oligomer is capable of hybridizing to its complement. The above reference by Southern describes a variety of oligomer arrays both regarding preparation and usage. One such array is disclosed on page 3, lines 9-12, made up of all possible sequences of a chosen length as enumerated, for example, on page 8, lines 21-35. These are hybridization arrays and so must contain oligomers which are hybridizable to their complement as well as content addressable in order to read out the result of any hybridization experiment. Such an array would correspond to a complex embodiment of the instant invention. A simpler type of set of oligomers is described in an experiment disclosed as starting on page 17 as Example 2 whereon only 2 single-stranded oligomers are present with each optionally hybridizable distinctively with its exactly complementary target. The presence of such complementary target or targets in a sample but yet single-stranded before hybridization to the array is yet another embodiment within the instant claim. On pages 17-20 a probe array of 19-mers is prepared to test 110 base possible sickle cell sequences. These samples contain single-stranded oligomers as well as at least one non-complementary sequence in the 110-mer beyond where it may hybridize to a 19-mer on the array thus also anticipating instant claim 26. It is

acknowledged that the citation of the disclosure of Southern regarding a computational composition as instantly claimed may be unexpected but this should serve to illustrate the vast breadth of instant claims 25 and 26.

This disclosure is objected to because it contains an embedded hyperlink and/or other form or browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. It is noted that the specification at page 60, lines 17-18, contains a hyperlink as discussed above. It is not understood how the replacement of the address for this hyperlink with the exact same address for the hyperlink removes this hyperlink. This objection is maintained.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703)308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703)308-4028.


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Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

December 15, 2000


ARDIN H. MARSCHEL
PRIMARY EXAMINER